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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,215	06/14/2001	Monika Junghans	WFG/12544	6039

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EXAMINER
SHEINBERG, MONIKA B

ART UNIT	PAPER NUMBER
1634	10

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,215	JUNGHANS ET AL.	
	Examiner	Art Unit	
	Monika B Sheinberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-33 and 35-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-33 and 35-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claim 1-35) in Paper No. 9, filed 24 October 2002, is acknowledged. In addition, it is noted that claim 36 was mistakenly left out of Group I, thus Group I entails claims 28-36. The traversal of Group I, is on the ground(s) that Group I, Group II and Group III share a common technical features. The restriction requirement is hereby withdrawn due to the Group II being drawn to the process of making the product of Group I; and Group III being drawn to at least one method of using the product of Group I. As such, claims 28-33 and 35-50 have been examined.

Claims 28-33 and 35-50 are pending.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 48-50 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28-33 and 35-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28, 37, and 48 are vague and indefinite due to the lack of clarity of the phrase "predominantly of arginine" line 3, 4, and 2, respectively. The metes and bounds of the parameters that define the term predominantly are unclear; for example, 90% arginine, poly-arginine, and so forth. As such claims 29-33, 35, 36, 38-47, 49 and 50 are also indefinite due to dependency from claims 28, 37, and 48.

Claims 29, 39, 49 and 50 recite the term "preferably" which is vague and indefinite. It is unclear what the metes and bounds of the parameters that define the term "preferably"; for example the utilized term in claim 49 merely states and does not require that the derivative is "preferably protamine sulfate or protamine chloride". No further limitations to the claims are provided by the use of this vague term. Clarification is requested for the parameters that define the metes and bounds of the term "preferably " via clearer claim wording.

Claims 48-50 provides for the use of a protein having a specified molecular weight, size and bound nucleic acid, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28-33 and 35-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolfert et al. (*Gene Therapy*, 1996) in view of Hanson et al. (WO 95/25809; 28-Sept-1995), and further in view of Wu et al. (WO 93/04701; 18-March-1993) and Zobel et al. (*Antisense Nuc. Acid. Drug Devel.*, 1997).

Wolfert et al. teaches polyelectrolyte complexes (or particles) consisting of polycations (poly-lysine) and nucleic acids, the method of producing the particles (claim 37), and a use of such particles (claim 48). The particles were determined to be more efficient in cellular access and entry as low molecular weight conjugates in which 3970 Da was demonstrated in figures 1 and 2 as required by claim 28. Figure 2 (p. 271) demonstrates the low molecular weight conjugates to be within the range required by claims 28 and 45; page 271 also states in line 7 the diameter to be 20-30nm. Figure 4 demonstrates the use of such particles in a test of cytotoxity. Wolfert et al suggests the alteration of electrostatic particle charges (claims 35, 38 and 46) due to "polyelectrolyte condensation could yield particles with extremely high charge density and possibly even increase toxicity" (p. 272, 2nd column, 2nd paragraph, lines 12-20).

Wolfert et al. does not teach the use of an arginine containing polycation (claims 28, 29, 37, 39, 40 and 48), single stranded DNA (claims 30, 41 and 50), a oligonucleotide of at least 5 nucleotides (claims 32, 43 and 50),

Hanson et al. demonstrates DNA compacted and complexed with a carrier molecule comprising a nucleic acid binding moiety such as polycations alone (p. 7, lines 30-35). The reference teaches the binding moieties to include arginine containing polycations, protamine (p. 23, 1st paragraph). The limitation of obtaining protamine from salmon sperm (claim 40) does not materially affect the consistency of the protamine utilized. The DNA used for complex formation is demonstrated to be single or double stranded DNA and 10 nucleotides in length (p. 23, 3rd paragraph).

Hanson et al. does not teach the use of DNA derivatives (claims 33, 44 and 50).

Wu et al. demonstrates molecular complexes or particles of oligonucleotides complexed to a poly- or oligonucleotide-binding agent such as a polycationic protein (abstract). The reference teaches "[s]uitable polycations are [...] poly-arginine, [...] protamines and the like" (p. 7, lines 24-27). The antisense oligodeoxynucleotides are demonstrated to be single stranded and include analogues or derivatives such as phosphorothioate oligonucleotides (p. 4, lines 20-26).

Wu et al. does not teach the surface electric charge of the particle within the ranges of –40mV to +40mV (claims 36 and 47).

Zobel et al. demonstrates the reduction of surface charge and electrostatic repulsion to produce a more compact nanoparticles consisting of a polycation and an oligonucleotide (p. 486-7, bridging paragraph) in order to increase cellular uptake efficiencies. Table 2 demonstrates these nanoparticles within the required range of –40mV to +40mV of claims 36 and 47, in addition to their relative particle diameters, which are also within the required range of claims 28 and 45.

It would have been *prima facia* obvious for one of ordinary skill in the art at the time the invention was made to have used the polycation, protamine, and single stranded DNA taught by Hanson et al in place of the poly-lysine for the production and use of polyelectrolyte complexes disclosed by Wolfert et al. Hanson et al. discloses particles and methods for the particle design of nucleic acids complexed with proteins for target cellular delivery just as Wolfert et al. One of ordinary skill in the art would have been motivated to utilize protamine as per the teachings of Wolfert et al. due to the reference's stating that "[c]onjugates formed using the lowest molecular weight polycations appear to be better tolerated than those formed with higher molecular weight ploy(L)lysine and they are proposed as candidates for further development" (p.273, 1st column, lines 9-13).

It would have further been obvious to have included the nucleic acid derivative features of the particles taught by Wu et al., as Wu et al. discloses the routine practice of the use of DNA analogues produced by "standard synthetic procedures" (p. 4, line 29) in of adjusting molecular stability for the reaching "target [cells] in effective concentrations" (lines 25-26). Wu et al.

discloses antisense oligonucleotides bound to polycationic proteins just as Wolfert et al. and Hanson et al (protamine use).

One would have been further motivated to alter surface electric charge as per the teaching of Zobel et al. with respect to the particles and methods taught by Wolfert et al. due to the suggestion that "polyelectrolyte condensation could yield particles with extremely high charge density and possibly even increase toxicity" (p. 272, 2nd column, 2nd paragraph, lines 12-20).

Conclusion

Claims 48-50 are rejected under 35 U.S.C. 101.

Claims 28-50 are rejected under 35 U.S.C. 112, second paragraph.

Claims 28-33 and 35-50 are rejected under 35 U.S.C. 103(a).

As such, no claim is allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 1 P.M to 8 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Chantae Dessau, whose telephone number is (703) 605-1237, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

January 27, 2003

Monika B. Sheinberg
Art Unit 1634

MBS

Jehanne Souaya

JEHANNE SOUAYA
PATENT EXAMINER

1/27/03